Stimulus dependence of the M100 latency in the age range 11-18 years

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1 Introduction

The latency of the major component of the auditory evoked neuromagnetic field, the M100 or N1m, is sensitive to acoustical and perceptual attributes of the presented stimulus [1-3]. In particular the latency depends upon stimulus intensity, frequency and spectral complexity. Thus latency variation has been proposed as an objective metric of hearing, complex sound processing and a number of clinical conditions in adults (e.g. tinnitus). Previous MEG studies have shown the 100ms component of the auditory evoked response to also have prolonged latency in children and teenagers [4]. Thus age may represent an additional factor in the description of latency variation, previously described, in some detail, in adults [2,3] as a function of stimulus attributes, such as stimulus intensity, acoustic structure and perceptual categorization. As such, latency measures in response to acoustic stimuli have a more complex interpretation in children. On the other hand, the age (development) dependent variation in evoked response latency may offer an objective instrument for the study and characterization of development in children and young adults. The accumulation of a normative database of evoked response latency as a function of stimulus acoustic complexity in children serves considerable value in the study of clinical sound processing and, in particular, developmental communication and language disorders, such as dyslexia, autism and attention deficit hyperactivity disorder.

2 Methods

13 healthy minors (age 11-17yrs) and 7 adult controls (age 25-35yrs) were studied. All studies were performed with the approval of the institutional committee on human research. Written informed consent was obtained from the subjects and their parent or legal guardian.

Auditory evoked neuromagnetic fields were collected using a 37-channel biomagnetometer (MAGNES^{TM}, BTi) from the contralateral hemisphere during monaural presentation of auditory stimuli. Recordings were made from both hemispheres. Stimuli were sinusoidal tones of varying frequency (100Hz-3kHz), harmonically-rich square wave tones (100Hz), and amplitude-modulated (AM) tones (1kHz carrier, 100Hz modulation frequency, 200% modulation depth leading to equal content energy peaks at 900Hz, 1kHz and 1100Hz). Stimuli were presented at 40dB sensation level after threshold detection levels were determined individually for each subject, for each ear, for each stimulus. Stimulus locked epochs of 600ms duration were acquired at a sampling rate of 2kHz/channel. At least 100 stimuli of each type were presented at a pseudo-randomized inter-stimulus interval of 1.0±0.1sec. Data were digitally filtered (passband 1-40Hz) and the M100 component was determined as that peak in evoked activity with maximum root mean square (r.m.s.) field amplitude (across sensor channels) occurring in the latency range 80-160ms post stimulus onset and satisfying a model-data correlation of $r>0.97$ using a single equivalent dipole model. The M100 latency was used as the dependent variable in these studies.

3 Results

Auditory evoked fields were elicited from all subjects, in response to all stimuli. M100 components were identified and ascribed to plausible sources in superior temporal gyrus. There was no systematic effect of M100 component field amplitude as a function of either stimulus type or subject age; evoked response amplitudes were of comparable magnitude to those obtained in adult subjects. However, in the age range 11-17 years, M100 latency in response to a 1kHz sinusoidal tone (Fig. 1) was inversely proportional to age (Left hemisphere: $r=0.72$, RH: $r=0.78$).

All subjects exhibited relatively prolonged latencies in response to lower frequencies (Fig. 2), consistent with previous adult data[1-3] with latency strongly proportional to 1/freq. ($r=0.5$ to $r=0.98$).

As has been repeatedly observed in adults, Left hemisphere (LH) latencies were later than right hemisphere (RH) responses ($p<0.001$). The dynamic range (Fig. 3) of latency prolongation (latency difference between 100Hz and 1kHz tones) did not vary with age (correlation with 1/age was r < 0.3), and was on average 20ms (vs. 24ms in the adults).

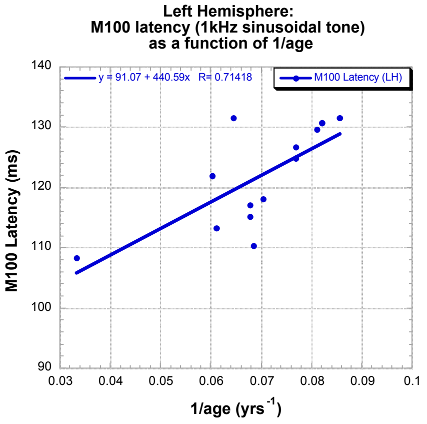

Figure 1: *M100 latency in response to a 1kHz tone varies inversely with age being ~20ms prolonged in the youngest child (age 11 yrs). Reference adult values are provided at a 1/age value of 0.033 (30 years). Similar results are found for right hemisphere responses.*

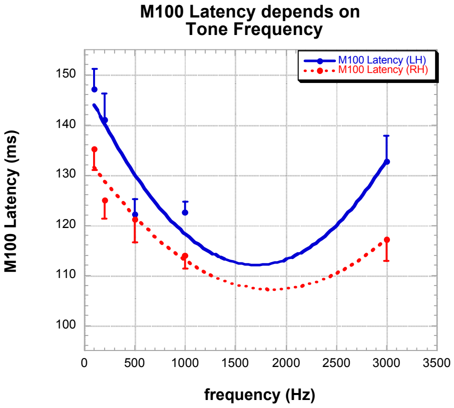

Figure 2: *As in adults, M100 latency is observed to vary with the frequency of stimulus tones, being quasi-parabolic [1]. Furthermore, left hemisphere responses are systematically prolonged versus their right hemisphere equivalents.*

Observations of latency correlates of spectral structure within stimuli also paralleled previous adult findings [2]. Latencies for low frequency (100Hz) square waves were less prolonged than for corresponding sinusoids (LH:8ms, RH:2ms). Amplitude modulated (AM)-tones with a carrier frequency of 1kHz and a modulation frequency of 100Hz gave rise to latencies slightly prolonged relative to a 1kHz sinusoid (LH: 4ms, RH=1ms).

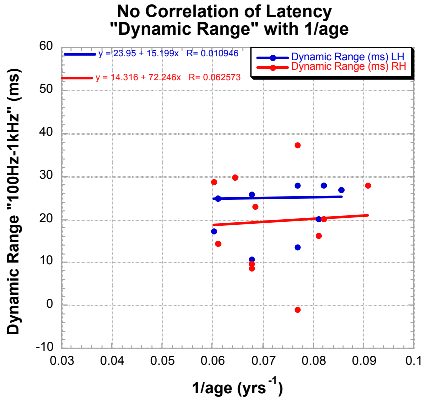

Figure 3: *The dynamic range of the M100 latency effect (the latency difference between responses to 100Hz vs. 1kHz tones did not change as a function of age and was not different between hemispheres.*

4 Discussion

The presence of frequency-dependence of M100 latency despite latency variation as a function of age suggests the tonochronic representation of frequency in evoked responses is established prior to the final stages of development (in which latencies arrive at the values observed in adulthood). Furthermore, since the dynamic range of the stimulus-frequency dependent latency shift did not vary as a function of age, one must assume that the mechanisms underlying this phenomenon are fully established by the age of 11years (the youngest subject in this study. Evidence for latency reflections of secondary spectral analysis (of harmonic structure, periodicity etc.) is already present in this age group. M100 latency variation with such a stimulus range is a potential measure of developmental delays in cortical processing of complex sounds. The inverse dependence of evoked response latency with subject age on the one hand represents an additional modulating variable on the dependent measure; on the other hand, this raises the possibility of exploiting latency measurements as objective indices of aspects of developmental status.

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